

Early yaws: a light microscopic study

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Abstract

This paper presents the light microscopic findings in biopsies of skin lesions from 45 patients, in whom a diagnosis of early yaws was suspected. In 27 cases typical light-microscopic features of yaws were observed, consisting of parakeratosis or crust containing exudate, marked acanthosis with widening and elongation of the rete ridges or pseudo-carcinomatous hyperplasia and spongiosis. Intraepidermal microabscesses consisting of polymorphonuclear leucocytes were frequently encountered. In a large majority a moderate to dense infiltrate was present, composed mainly of lymphocytes and plasma cells. Vascular changes consisted of only slight endothelial cell proliferation and thickening of vessel walls. Steiner staining revealed the presence of treponemes in the epidermis in 23 of 27 cases. Remarkably, clusters of treponemes were also seen in the papillary dermis in three out of 23 cases. Seven other cases were strongly suggestive of yaws. Other histopathological diagnoses were made in 6 patients, due to the simultaneous occurrence of other skin diseases. The remaining five specimens did not contain enough tissue to allow conclusions to be made.

Introduction

Yaws, caused by *Treponema pallidum* subsp. *pertenue* (*T. pertenue*), is a chronic infectious disease found in rural areas with tropical, very warm, humid climates. The disease is transmitted nonvenereally by skin-to-skin contact, mainly among toddlers and infants.¹⁻² Early lesions are mainly restricted to the skin and mucous membranes. In some patients the disease

progresses to the late stage, in which destructive changes of skin, bone, cartilage and soft tissues are notorious.

An alarming resurgence of yaws has been reported,³ specifically in West and Central Africa. In Southeast Asia there are also many residual foci.⁴⁻⁵ During investigations in 1988 cases of early infectious yaws were observed in West Sumatra, Indonesia.⁶

In 1957 Hasselmann pointed to the remarkable epidermotropic character of *T. pertenue*.⁷ Only a limited number of studies on the microscopic aspects of yaws had been published before 1940. Conclusions were based on material obtained from a limited number of patients. During the last 30 years the histological features of early yaws have not been studied intensively.

In this article we discuss the histological features of early yaws. A light-microscopic study of skin biopsies from 45 patients was performed.

Materials and methods

Subjects of this study were 45 patients, 11 females and 34 males, all presenting with skin lesions. In all persons a diagnosis of early infectious yaws was suspected on clinical and epidemiological grounds. Mean age of the patients was 7.6 years (range: 1-25 years). They were examined between 18 November and 25 November, 1988, in six different regional Health Centres in rural areas in West Sumatra, Indonesia. According to the Centre for Disease Control (CDC) in Padang, yaws is hyperendemic and venereal syphilis is not encountered in these remote regions in Sumatra (personal communication).

After clinical examination, dark-field examination of exudates of skin lesions of 41 patients was performed and blood samples were collected by venipuncture from 42 patients. In The Netherlands the Venereal Disease Research Laboratory (VDRL) test, the *Treponema pallidum* haemagglutination assay (TPHA) and the fluorescent treponemal antibody absorption (FTA-ABS) test were performed.

Biopsy specimens were taken from suspect skin lesions. A part of the biopsy tissue was fixed in phosphate-buffered 4% formaldehyde solution. Another part was frozen immediately and specimens were kept in dry ice. They were transported in dry ice from Indonesia to The Netherlands. In Rotterdam,

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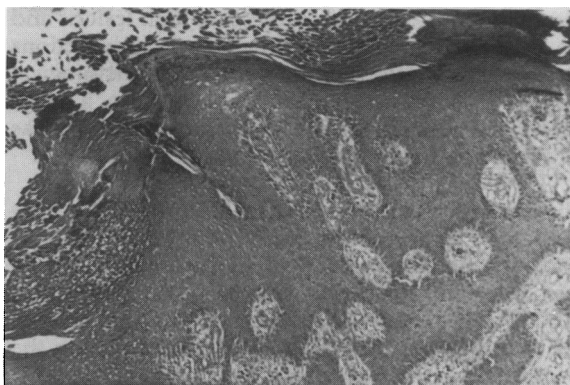


Figure 1 Papillomatous lesion: marked acanthosis and spongiosis. Infiltrate consisting mainly of lymphocytes and plasma cells (haematoxylin-azophloxin, 120 \times).

routine staining was performed with haematoxylin-azophloxin. To study the presence and localisation of treponemes in the biopsies, the histochemical silver staining method according to Steiner⁸ was applied.

Results

The 45 patients presented with skin lesions characteristic of yaws. Papillomatous and papulosquamous skin lesions, often ulcerated and covered with crusts, were by far the most frequent. The large majority of all skin lesions were located on the lower extremities (especially the lower legs and arms), which often form the portal of entry for *T. pertenue*.¹⁻²

Of 42 persons tested serologically, all blood samples except one reacted positive in one or more of the VDRL, TPHA and FTA-ABS tests. The seronegative patient presented with an ulcer on the left leg (dark-field examination negative, Steiner staining negative) for which no cause could be detected.

Dark-field examination showed the presence of treponemes in 24 out of 41 cases.

In 23 patients light microscopy revealed the unmistakable presence of epidermal changes, consist-

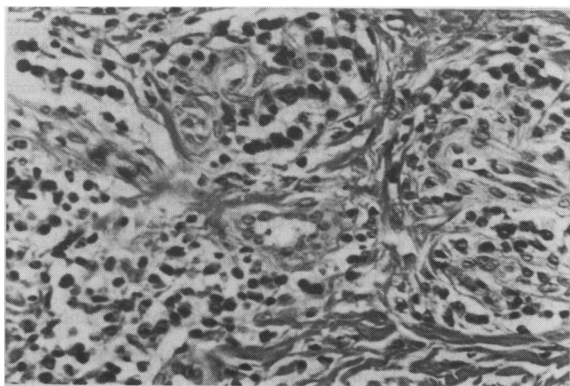


Figure 2 Only mildly affected blood vessels: slight endothelial cell proliferation and thickening of vessel walls (h-a, 420 \times).

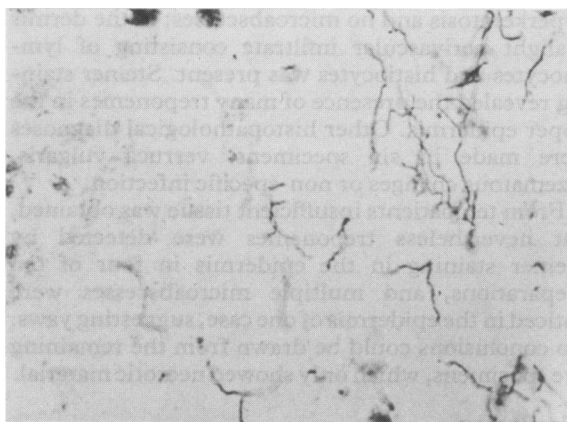


Figure 3 Numerous treponemes are visualised in the epidermis (Steiner staining method, 580 \times).

ing of parakeratosis or crust-containing exudate, inflammatory cells and fibrin. There was marked acanthosis with widening and elongation of the rete ridges or pseudocarcinomatous hyperplasia and spongiosis (fig 1). Collections of polymorphonuclear leucocytes were present within the epidermis in all 23 cases. The upper dermis showed marked oedema, dilated capillaries and cellular infiltration in all cases. An infiltrate composed of plasma cells and lymphocytes was observed in all 23 cases; histiocytes were present in four of 23 cases and polymorphonuclear leucocytes were seen in two. In addition, eosinophils were present in the infiltrate in three cases. The cellular infiltrate in the deeper dermis consisted mainly of plasma cells and was located around the blood vessels. Of two of 23 cases a mild infiltrate was observed; a moderate infiltrate was seen in eleven and a heavy infiltrate in ten cases. The capillaries in all dermal layers revealed only slight endothelial cell proliferation and thickening of vessel walls (fig 2) in all except one case, in which no vascular changes were present. No thrombosis or rupture of vessels was observed.

In all 23 cases foci of treponemes could be demonstrated by the Steiner staining method in the epidermis (8 in the upper epidermis and 15 throughout the epidermis) and in only three cases microorganisms were also seen in the papillary dermis. In several cases extensive clusters of treponemes were noticed in the epidermis (fig 3).

In four cases the histological picture strongly suggested yaws, but this was not confirmed by silver staining. Scar tissue was found in one case, in which dermal fibrosis with a slight inflammatory infiltrate was observed. This could have been the remnant of a healed yaws lesion, since dark-field examination of the exudate of other skin lesions revealed the presence of many motile treponemes and serological tests were strongly positive. In one case an atypical picture was seen: irregular acanthosis, only slight

hyperkeratosis and no microabscesses; in the dermis a slight perivascular infiltrate consisting of lymphocytes and histiocytes was present. Steiner staining revealed the presence of many treponemes in the upper epidermis. Other histopathological diagnoses were made in six specimens: verruca vulgaris, eczematous changes or non-specific infection.

From ten patients insufficient tissue was obtained, but nevertheless treponemes were detected by Steiner staining in the epidermis in four of ten preparations, and multiple microabscesses were noticed in the epidermis of one case, suggesting yaws. No conclusions could be drawn from the remaining five specimens, which only showed necrotic material.

Discussion

In yaws, a primary stage and a secondary stage were discerned, although these stages can overlap. Nowadays the term early yaws is used, comprising the primary and secondary stage.⁹

According to the old literature on the histopathology of yaws, in the early stage lesion epidermal hyperplasia and papillomatosis are pronounced, often with focal spongiosis.¹⁰⁻¹² Frequently microabscesses are present within the epidermis (neutrophils, migrating into the epidermis). A dense dermal infiltrate consists mainly of plasma cells,¹² but can also contain lymphocytes, neutrophils, histiocytes, and eosinophils. Little or no proliferation of endothelial cells is present, and obliterative changes in the vessels are not encountered. This is in contrast with the picture in venereal syphilis, in which involvement of blood vessels is much more pronounced, although not consistently present.¹¹

The pathological findings in the early yaws lesions we describe, are largely similar to those described many years ago. However, in our material blood vessels were involved in most cases, but endothelial proliferation was only slight. Intraepidermal microabscesses were present in most cases. The infiltrate was moderate to dense, and consisted mainly of plasma cells and lymphocytes, and occasionally of neutrophils, histiocytes and eosinophils. The epidermotropic character of *T. pertenue* was obvious, as studied using Steiner silver staining. In most cases the microorganisms were detected between epidermal cells, in the upper regions of the epidermis or throughout the epidermis, although in three preparations treponemes were present in the upper dermis too. In some of our preparations of early yaws a microscopic diagnosis was doubtful. Other bacterial (super-) infections made the picture of yaws less clear. In a few cases skin lesions strongly suggested yaws clinically, but microscopically another diagnosis was made, such as eczema, verruca vulgaris or non-specific bacterial infection, probably due to the simultaneous occurrence of other skin infections.

In conclusion, in this study the microscopic picture of early stage skin lesions was frequently characteristic. Owing to the variety in the clinical presenta-

tion of yaws, the friable character of skin lesions and the frequent occurrence of other bacterial infections simultaneously affecting the skin, a clear histological picture is not always seen. However, in a large majority of patients the clinical diagnosis of yaws was confirmed by histopathological examination.

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